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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,975	04/28/2005	Yasumasa Mitani	20078.0005USWO	4649

52835 7590 08/15/2007
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EXAMINER

BERTAGNA, ANGELA MARIE

ART UNIT	PAPER NUMBER
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1637

MAIL DATE	DELIVERY MODE
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08/15/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,975	MITANI ET AL.	
	Examiner	Art Unit	
	Angela Bertagna	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 18-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☒ Claim(s) 7 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 April 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/28/05; 7/11/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-17, in the reply filed on January 24, 2007 is acknowledged.

Claims 18-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Election was made **without** traverse in the reply filed on January 24, 2007.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

3. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

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The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract of the disclosure is objected to because it uses legal phraseology, specifically, "said". Correction is required. See MPEP § 608.01(b).

Claim Objections

4. Claim 7 is objected to because of the following informalities: This claim appears to contain a typographical error, because it recites "betains" in line 2. It appears that "betaine" was intended. Appropriate correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-7 and 9-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Rabbani et al. (EP 0 971 039 A2; cited on IDS).

Regarding claim 1, Rabbani teaches a method for amplifying a nucleic acid comprising:

(a) providing a primer comprising in its 3' end portion a sequence (Ac') that hybridizes to a sequence (A) in the 3' end portion of the target nucleic acid, and a sequence (B') located 5' of (Ac') that hybridizes to the complementary sequence (Bc) of a sequence (B) positioned 5' of

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sequence (A) in the target nucleic acid (see Example 1 on page 21, where the FC and RC primers of Rabbani are taught; see also Figure 1 for a schematic of the primers binding to a target)

wherein in the absence of an intervening sequence between (Ac') and (B'), $(X-Y)/X$ is between -1.00 and 1.00 , where X is the number of bases in sequence (Ac') and Y is the number of bases in the region flanked by sequences (A) and (B) on the target nucleic acid sequence (see Example 1 on page 21, paragraphs 117-118, where the FC and RC primers have an (Ac') region of 29 or 30 nucleotides and the region flanked by sequences A and B is 0 nucleotides, since there is no intervening sequence between them. Therefore, $(X-Y)/X = (29-0)/29 = 1$)

(b) providing a template nucleic acid (page 21, paragraphs 117 and 120)

(c) annealing the primer to the template and synthesizing a nucleic acid sequence complementary to the target by primer extension (see paragraph 120-121 and also Figure 1, steps 1-2)

(d) hybridizing sequence (B') with sequence (Bc) on the newly synthesized strand, thereby allowing sequence (A) on the target strand to be single-stranded (see Figure 1, step 3)

(e) annealing another primer of step (a) to the single-stranded sequence (A) on the target generated in step (d) and conducting a strand displacement reaction, thereby displacing the complementary nucleic acid synthesized in step (c) (see Figure 1, steps 4-5).

Regarding claim 2, Rabbani teaches that the double-stranded nucleic acid obtained in step (e) is used repeatedly in step (d) (see Figure 1 and paragraph 47).

Regarding claims 3 and 12, Rabbani teaches that the method is conducted isothermally (see paragraphs 46, 51, and 121).

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Regarding claims 4 and 13, Rabbani teaches use of the Bst DNA polymerase, which has strand-displacing ability (paragraph 120).

Regarding claims 5 and 14, Rabbani teaches that the method further comprises a step of synthesizing cDNA with a reverse transcriptase from an RNA template (paragraph 111).

Regarding claims 6, 7, 15, and 16, Rabbani teaches conducting the method in the presence of a melting temperature adjusting agent, specifically formamide or DMSO (paragraph 39).

Regarding claim 9, Rabbani teaches a method for amplifying a target nucleic acid in a double-stranded template nucleic acid comprising:

(a) providing a first primer comprising in its 3' end portion a sequence (Ac') that hybridizes to a sequence (A) in the 3' end portion of the target nucleic acid, and a sequence (B') located 5' of (Ac') that hybridizes to the complementary sequence (Bc) of a sequence (B) positioned 5' of sequence (A) in the target nucleic acid (see Example 1 on page 21, where the FC and RC primers of Rabbani are taught; see also Figure 1 for a schematic of the primers binding to a target)

wherein in the absence of an intervening sequence between (Ac') and (B'), $(X-Y)/X$ is between -1.00 and 1.00, where X is the number of bases in sequence (Ac') and Y is the number of bases in the region flanked by sequences (A) and (B) on the target nucleic acid sequence (see Example 1 on page 21, paragraphs 117-118, where the FC and RC primers have an (Ac') region of 29 or 30 nucleotides and the region flanked by sequences A and B is 0 nucleotides, since there is no intervening sequence between them. Therefore, $(X-Y)/X = (29-0)/29 = 1$)

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(b) providing a second primer comprising in its 3' end portion a sequence (Cc') that hybridizes to a sequence (C) in the 3' end portion of the target nucleic acid, and a sequence (D') located 5' of (Cc') that hybridizes to the complementary sequence (Dc) of a sequence (D) positioned 5' of sequence (C) in the target nucleic acid (see Example 1 on page 21, where the FC and RC primers of Rabbani are taught; see also Figure 1 for a schematic of the primers binding to a target)

wherein in the absence of an intervening sequence between (Cc') and (D'), $(X-Y)/X$ is between -1.00 and 1.00 , where X is the number of bases in sequence (Cc') and Y is the number of bases in the region flanked by sequences (C) and (D) on the target nucleic acid sequence (see Example 1 on page 21, paragraphs 117-118, where the FC and RC primers have an (Cc') region of 29 or 30 nucleotides and the region flanked by sequences C and D is 0 nucleotides, since there is no intervening sequence between them. Therefore, $(X-Y)/X = (29-0)/29 = 1$)

(c) providing a double-stranded template nucleic acid consisting of the first and second template strands (paragraphs 77 and 117)

(d) annealing the first and second primers to the first and second template nucleic acids and synthesizing complementary strands via primer extension (paragraphs 117-118; see Figure 1, steps 1-2 for a schematic of how the primers anneal to the target. Although Figure 1 shows the reactions occurring on only one strand, when both the FC and RC primer are used with a double-stranded template as taught by Rabbani in Example 1, each of the primers inherently undergoes the reactions outlined in Figure 1 on a different strand of the template; see also paragraph 77, where Rabbani expressly teaches conducting the amplification method using two stem-loop

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primers each of which is complementary to a different strand of a double-stranded DNA template)

(e) hybridizing the sequences (B') and (D') with the newly synthesized sequences (Bc) and (Dc); respectively, thereby making sequences (A) and (C) single stranded (see Figure 1, step 3 and paragraph 118; see also paragraph 77)

(f) annealing primers having the same sequence as the first and second primers of step (a) to sequences (A) and (C) obtained in step (e) above and conducting strand displacement polymerization to displace the complementary strands obtained in step (d) and synthesize new complementary strands (see paragraph 118 and Figure 1, steps 4-5; see also paragraph 77).

Regarding claim 10, Rabbani teaches that the double-stranded nucleic acids obtained in step (f) are repeatedly used in step (e) (see paragraphs 77 & 118; see also Figure 1).

Regarding claim 11, Rabbani teaches that the first and second complementary nucleic acids obtained in step (f) as single-stranded nucleic acids are used repeatedly as template nucleic acids in step (d) (see Figure 2, step 4 and paragraph 77).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 8 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rabbani et al. (EP 0 971 039 A2; cited on IDS) in view of Kool, E.T. (Current Opinion in Chemical Biology (2000) 4: 602-608).

Rabbani teaches the method of claims 1-7 and 9-16, as discussed above.

Rabbani does not teach that target nucleic acid sequence in the template nucleic acid comprises non-natural nucleotides as required by claims 8 and 17.

Kool teaches methods of using modified DNA templates as substrates for DNA polymerases. Kool teaches that DNA polymerases can accept synthetic modifications to the template or newly synthesized strand (page 602, column 2). Kool further teaches that templates containing nucleotides with altered hydrogen-bonding capabilities may be amplified by DNA polymerase (page 604). Kool teaches that the presence of these non-native nucleotides in the template strand directs non-specific incorporation of any of the four natural bases into the newly synthesized strand, which is useful for mutagenesis (page 604).

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It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to conduct the amplification method taught by Rabbani using a template containing non-natural nucleotide. An ordinary practitioner would have been motivated to do so, since Kool taught that the inclusion of such nucleotides in the template strand was useful for mutagenesis applications (see page 604). Since Kool further taught a number of specific examples of non-native nucleotides that could be recognized and amplified by DNA polymerases (see pages 604-606), an ordinary practitioner would have had a reasonable expectation of success in utilizing a template containing non-native nucleotides in the method of Rabbani. Thus, the methods of claims 8 and 17 are prima facie obvious in view of the combined teachings of Rabbani and Kool.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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10. Claims 1-4, 6, 7, 9-13, 15 and 16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8-12, 15, and 20-23 of copending Application No. 10/583,706. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 8 and 15 of the '706 application recite all of the limitations of the instant claims 1, 2, and 9-11, and therefore, anticipate these claims. The limitations of the instant claims 3, 4, 6, 7, 12, 13, 15, and 16 are recited in claims 9-12 and 20-23 of the '706 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are currently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Angela Bertagna whose telephone number is 571-272-8291. The examiner can normally be reached on M-F, 7:30 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Angela Bertagna
Art Unit 1637 *AMB*
August 8, 2007

amb

JF
JEFFREY FREDMAN
PRIMARY EXAMINER

8/1/07